IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	Art Unit: 1614
	)	
Olle KORSGREN et al	)	Examiner: Donna Jagoe
	)	
Appln. No.: 09/890,936	)	Washington, D.C.
	)	
Date Filed: November 7, 2001	)	Confirmation No. 9165
	)	
For: NOVEL USE WITHIN TRANSPLANTATION SURGERY	)	ATTY.'S DOCKET: KORSGREN=1

THIRD DECLARATION OF ROLF LARSSON

(1) I, Rolf Larsson, hereby solemnly declare as follows:

(2) I am the same Rolf Larsson who is a co-inventor of the invention of the above-identified application, and a co-applicant of this application; and the same Rolf Larsson who executed first and second declarations respectively filed in the present application on March 2, 2004, and April 4, 2007.

(3) I confirm the accuracy of what is stated in those earlier declarations, except for one inadvertent error: while Olle Korsgren and Bo Nilsson have both M.D. and Ph.D. degrees, I do not have an M.D. degree. This was incorrectly stated in the second declaration but was correctly stated in the first declaration.

(4) I attended, along with our U.S. attorney, an interview in the United States Patent and Trademark Office on June 28, 2007. Since that time, the examiner has issued another rejection, mailed August 9, 2007, and I have studied that Office Action. In that Office Action, the examiner states that the concept of coating individual islet cells separately with a heparin coating is a concept that was not present in the specification as originally filed. This conclusion by the examiner is incorrect.

(5) The specification uses the nomenclature "isolated islets", which refers to islets being isolated from the pancreas according to well-established procedure. Such procedure produces individual islets as is readily observed by an ordinary microscope and well appreciated by workers in the present field. An individual islet is illustrated by a photomicrograph in our second declaration at page 4, Fig. 2, which was (as stated in the second declaration) prepared in our laboratory. As there stated (bottom of page 3 and top of page 4 of our second declaration), Fig. 2 "shows one islet cell coated with heparin according to our invention and examined by confocal microscopy using fluorescently labelled antithrombin that binds to heparin. It is evident that the coating follows the contour of the cell and is in direct contact with the cell surface".

(6) Based on my experience and my knowledge, I know as fact that the isolated islets are individually coated with heparin according to our invention. Furthermore, I state with utmost confidence that anyone skilled in the art will readily appreciate that "isolated islets" and "individually isolated islets" are synonymous.

(7) The new Office Action repeats rejections based on Wagner et al and on Soon-Shiong et al. I understand that these rejections are based on the examiner's position that what is recited in the claims is not new. These rejections are incorrect because our process as set forth in claims 4, 8 and 11 is new and is quite different from both Wagner and Soon-Shiong.

(8) The examiner refers to claim 8 of Wagner, but claim 8 does not disclose the use of heparin or anything similar to heparin. Claim 8 of Wagner refers to a product characterized by an immobilization system of a porous or hollow material.

(9) Claim 7 of Wagner does mention heparin (among other possibilities) "used to antagonize agglomeration." Other than claim 7, Wagner does not mention heparin. Wagner does not describe how heparin might be used in the Wagner system. The examiner says on page 8 of the Office Action that in Wagner "the islet cells are combined with heparin and

encapsulated with a polymer such as alginate", but there is no such disclosure which I have been able to find in Wagner.

(10) And on page 7, Wagner states: "Most of the microcapsules of a diameter of half a millimeter have a volume several times larger than that of the islets of Langerhans, which are 50-300 μm in size."

(11) The examiner says that "if the cells are microencapsulated, they are first mixed with anticoagulant material, thus anticipated the claims of the instant application". Not only can I find no such disclosure in Wagner, but what the examiner states is basically impossible as pointed out during the aforementioned interview. If the cells were first mixed with an anticoagulant and then encapsulated, the anticoagulant could not function because the anticoagulant would be sealed within the microcapsule.

(12) Soon-Shiong discloses, as indicated by the title of this patent, "microcapsules prepared from cross-linkable polysaccharides, polycations and/or lipids and use therefor". There is no doubt that cross-linking is intended and is provided in the formation of the microcapsule shell in Soon-Shiong. To the contrary, heparin, as well as Corline Heparin Conjugate, the preferred heparin material used in the present invention, is a water soluble substance that is adsorbed onto the islet surface as shown in Fig. 2 at page 4

of the aforementioned second declaration, and there is no cross-linking and no ability of the heparin or Corline Heparin Conjugate to cross link.

(13) While Soon-Shiong mentions heparin as a possible agent to prevent agglomeration of the microcapsules, it does not disclose the possibility that heparin may be applied directly to the surface of the islets.

(14) Newly relied upon Nomura et al discloses only the use of heparin administered systemically. Systemic administration of heparin is likely to generate bleeding complications, and has nothing to do with our invention which relates to the use of surface-bound heparin which acts locally at the surface of the islets thus eliminating bleeding complications.

(15) New applied Couser et al addresses another aspect of islet transplantation, namely systemic administration of a drug (sCR1) which is contrary to the present invention relating to the use of surface-bound heparin which acts locally at the surface of the islets.

I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are

punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 2007-11-29 By _____
Rolf LARSSON

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